weeks in the range of 6.25 to 50 mg b.i.d. (or equivalent level of placebo). The maintenance phase of each study ranged from six to 12 months, after which patients had the option of receiving open-label carvedilol in an extension study.

Results

The analysis presented below corresponds to the data set on which the DSMB made the recommendation to terminate the trials. Included in this intent-to-treat analysis are all patients enrolled in the U.S. trials as of Jan. 20, 1995; 624 receiving carvedilol and 356 placebo. An analysis of baseline patient characteristics (Table 1) shows good balance between the randomized groups.

TABLE 1

US Carvedilol Heart Failure Trials - Baseline Characteristics

Characteristic	Placebo (n = 356)	Carvedilol (n = 624)
Age, mean ± SD (years)	59.9 ± 11.7	58.8 ± 11.8
Sex (% men)	62%	62%
Etiology (% ischemic)	43%	40%
Severity of CHF		
Class II	41%	41%
Class III–IV	40%	39%
Unknown	19%	20%
LV ejection fraction, mean ± SD	0.22 ± 0.07	0.23 ± 0.08
6 Minute walk (m ± SD)	373 ± 88	379 ± 81
Blood pressure (mmHg)	115/73	115/73
Heart rate (bpm ± SD)	85 ± 13	86 ± 13

The overall mortality results for the program are shown in Table 2. All deaths that occurred during the intent-to-treat period are included. Treatment with carvedilol resulted in a 67% reduction in the risk of all-cause mortality. Analysis of mortality by certain baseline characteristics shows this to be a broad effect regardless of severity or etiology of CHF. The effect was uniform in patients with mild heart failure or moderate to severe heart failure. Similarly, the mortality reduction was equivalent in patients with ischemic or non-ischemic heart failure.

TABLE 2

Evaluation of Mortality in US Carvedilol CHF Studies

	Carvedilol	Placebo	Risk Reduction (95% CI)	p value*
All Cause Mortality	18/624 (2.9%)	29/356 (8.2%)	67% (42–81)	<0.0001
Class II CHF	7/361 (1.9%)	12/202 (5.9%)	68% (20–97)	0.015
Class III–IV CHF	11/263 (4.2%)	17/154 (11.0%)	66% (30–84)	0.004
Ischemic Etiology	10/311 (3.2%)	16/178 (8.9%)	67% (32–85)	0.003

TABLE 2-continued

Evaluation of Mortality in US Carvedilol CHF Studies

	Carvedilol	Placebo	Risk Reduction (95% CI)	p value*
Non-Ischemic Etiology	8/313 (2.5%)	13/178 (7.3%)	67% (20–86)	0.014

*Cochran-Mantel-Haensel Analysis

Conclusion

The U.S. Phase III trials were prospectively designed to evaluate the effects of carvedilol on the wellbeing and survival of patients with congestive heart failure. Twenty-five months after the program was initiated, the independent Data and Safety Monitoring Board recommended that the trials be terminated because of a 67% reduction in all-cause mortality. This effect was independent of the underlying severity or etiology of heart failure.

The foregoing is illustrative of the use of the compounds of this invention. This invention, however, is not limited to the precise embodiment described herein, but encompasses all modifications within the scope of the claims which follow.

What is claimed is:

1. A method of decreasing mortality caused by congestive heart failure in a patient in need thereof which comprises administering a therapeutically acceptable amount of carvedilol in conjunction with one or more other therapeutic agents, said agents being selected from the group consisting of an angiotensin converting enzyme inhibitor (ACE), a diuretic, and digoxin.

2. A method according to claim 1 which comprises administering carvedilol in a dosage range of from about 3.125 to about 50 mg given twice daily.

3. A method according to claim 1 which comprises administering carvedilol in a maintenance dose of about 25 mg given twice daily.

4. A method according to claim 1 which comprises administering carvedilol in a maintenance dose of between about 25 mg and about 50 mg given twice daily to patients whose weight exceeds about 85 kg.

5. A method according to claim 1 which comprises administering carvedilol in a maintenance dose of about 50 mg given twice daily in patients whose weight exceed about 85 kg.

6. A method according to claim 1 wherein said ACE inhibitor is captopril, lisinopril, or enalapril, or any pharmaceutically acceptable salt thereof.

7. A method according to claim 1 wherein said diuretic is hydrochlorothiazide or furosemide, or any pharmaceutically acceptable salt thereof.

* * * * *